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Award Number: W81XWH-10-1-0451

TITLE: Enhancing the Phagocytic Clearance of Apoptotic Cells to Control Breast Carcinoma Progression

PRINCIPAL INVESTIGATOR: Michael R. Elliott

CONTRACTING ORGANIZATION: University of Rochester
Rochester, NY 14627

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14. ABSTRACT

Macrophages have emerged as a key cell type influencing the initiation, progression and metastasis of breast cancer. Their impact on carcinogenesis is largely understood through their role in promoting a pro- or anti-inflammatory milieu. The phagocytosis of apoptotic cells by macrophages, a chief function of these cells, greatly influences the inflammatory status of macrophages. Despite the abundance of both macrophages and apoptotic cells in mammary tumors, little is known about how these cells interact in the tumor environment. Understanding how macrophages respond to apoptotic cells during the engulfment process should reveal important information on how this critical cell type influences the development and progression of breast cancer, with implications for future prevention and treatment strategies targeting macrophages. The aims of this study are designed to directly test the role of nucleotides as apoptotic cell find-me signals in the recruitment of macrophages to developing mammary tumors. The primary hypothesis is that the efficient recruitment and clearance of apoptotic cells by macrophages reduces inflammation caused by potentially necrotic cells that can spur tumor growth.

15. SUBJECT TERMS
cancer, apoptosis, phagocytosis, purinergic signaling

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AWARD: BC097647 (W81XWH-10-1-0451)
TITLE: Enhancing the phagocytic clearance of apoptotic cells to control breast carcinoma progression
PI: Michael R. Elliott, Ph.D.

INTRODUCTION: Macrophages have emerged as a key cell type influencing the initiation, progression and metastasis of breast cancer. Their impact on carcinogenesis is largely understood through their role in promoting a pro- or anti-inflammatory milieu. The phagocytosis of apoptotic cells by macrophages, a chief function of these cells, greatly influences the inflammatory status of macrophages. Despite the abundance of both macrophages and apoptotic cells in mammary tumors, little is known about how these cells interact in the tumor environment. Understanding how macrophages respond to apoptotic cells during the engulfment process should reveal important information on how this critical cell type influences the development and progression of breast cancer, with implications for future prevention and treatment strategies targeting macrophages. The aims of this study are designed to directly test the role of nucleotides as apoptotic cell find-me signals in the recruitment of macrophages to developing mammary tumors. The primary hypothesis is that the efficient recruitment and clearance of apoptotic cells by macrophages reduces inflammation caused by potentially necrotic cells that can spur tumor growth.

BODY: As per the revised SOW dated March 7, 2011 revision, all work is to be completed at PI's current institution (University of Rochester Medical Center). Thus, there are no findings from this study to report as yet.

KEY RESEARCH ACCOMPLISHMENTS: None pertaining to current SOW.

REPORTABLE OUTCOMES: This funding source was acknowledged in a review article by the PI (see Reference below).

CONCLUSION: N/A

REFERENCES:

Elliott, M.R. & Ravichandran, K.S. ELMO1 signaling in apoptotic germ cell clearance and spermatogenesis. *Ann. N. Y. Acad. Sci.* **1209**, 30-36 (2010).

APPENDICES: N/A

SUPPORTING DATA: N/A